

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2005/001298

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 A61K31/7088 A61P25/00 C07K14/71 C12Q1/68  
G01N33/50 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/000656 A (ISIS PHARMACEUTICALS, INC. (US); MURRAY SUSAN F.; WYATT JACQUELINE R.) 3 January 2003 (2003-01-03) page 14 page 88 - page 93; tables 1,2 the whole document	1-7
X	ZHAO J. ET AL.: "Abrogation of transforming growth factor-beta type II receptor stimulates embryonic mouse lung branching morphogenesis in culture" DEVELOPMENTAL BIOLOGY, ACADEMIC PRESS, NEW YORK, NY, US, vol. 180, 1996, pages 242-257, XP002957237 ISSN: 0012-1606 the whole document	1-4

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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## ° Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

15 September 2005

Date of mailing of the international search report

30 SEP 2005

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HIGASHIYAMA M. ET AL.: "Inhibition by Transforming Growth Factor-beta1 of the cellular action of Arginine Vasopressin in cultured rat glomerular mesangial cells" HYPERTENSION RESEARCH, vol. 22, no. 3, September 1999 (1999-09), pages 173-180, XP008036314 the whole document	1-4
Y	WO 93/19783 A (WHITTIER INSTITUTE FOR DIABETES & ENDOCRINOLOGY (US); LOGAN A; BAIRD A) 14 October 1993 (1993-10-14) the whole document	8-10
Y	DE GROOT C.J.A. ET AL.: "Expression of Transforming Growth Factor (TGF)-beta1, -beta2, and -beta3 isoforms and TGF-beta type I and type II receptors in Multiple Sclerosis lesions and human adult astrocytes cultures" JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, vol. 58, no. 2, February 1999 (1999-02), pages 174-187, XP008036355	8-11
A	page 186, left-hand column the whole document	10
A	KRIEGLSTEIN K. ET AL.: "Reduction of endogenous Transforming Growth Factor beta prevents ontogenetic neuron death" NATURE NEUROSCIENCE, vol. 3, no. 11, November 2000 (2000-11), pages 1085-1090, XP002298764 the whole document	8-10
Y	WYSS-CORAY T. ET AL.: "Chronic overproduction of Transforming Growth Factor-beta1 by astrocytes promotes Alzheimer's disease-like microvascular degeneration in transgenic mice" AMERICAN JOURNAL OF PATHOLOGY, vol. 156, no. 1, January 2000 (2000-01), pages 139-150, XP002298920 cited in the application the whole document	8-11
Y	LESNÉ S. ET AL.: "Transforming Growth Factor-beta1 potentiates Amyloid-beta generation in astrocytes and in transgenic mice" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 20, 16 May 2003 (2003-05-16), pages 18408-18418, XP002298507 the whole document	8-11
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## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SANCHEZ-CAPELO A. ET AL.: "Transforming Growth Factor beta1 overexpression in the nigrostriatal system increases the dopaminergic deficit of MPTP mice" MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 23, 2003, pages 614-625, XP002298508 the whole document	8-11
Y	BAKER C.A. ET AL.: "Microglial activation varies in different models of Creutzfeldt-Jakob disease" JOURNAL OF VIROLOGY, vol. 73, no. 6, June 1999 (1999-06), pages 5089-5097, XP008036207 cited in the application page 5094, right-hand column	8-11
A	EP 1 133 988 A (BIOGNOSTIK GESELLSCHAFT BIOMELEKULARE DIAGNOSTIK MBH; SCHLINGENSIEPEN) 19 September 2001 (2001-09-19) page 5; examples 2,3 page 7, line 24	8-10
A	YU W. ET AL.: "Evidence for role of Transforming Growth Factor-beta in RRR-alpha-Tocopheryl Succinate-induced apoptosis of human MDA-MB-435 breast cancer cells" NUTRITION AND CANCER, vol. 27, no. 3, 1997, pages 267-278, XP008046854	
A	LUO X. ET AL.: "The expression of Smads in human endometrium and regulation and induction in endometrial epithelial and stromal cells by Transforming Growth Factor-beta" THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM, vol. 88, no. 10, 2003, pages 4967-4976, XP002328270	
A	LENFERINK A.E.G. ET AL.: "Expression of TGF-beta type II receptor antisense RNA impairs TGF-beta1 signaling in vitro and promotes mammary gland differentiation in vivo" INTERNATIONAL JOURNAL OF CANCER, vol. 107, 2003, pages 919-928, XP008036311	
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## INTERNATIONAL SEARCH REPORT

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PCT/EP2005/001298

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MILNER N. ET AL.: "Selecting effective . antisense reagents on combinatorial . oligonucleotide arrays" NATURE BIOTECHNOLOGY, vol. 15, June 1997 (1997-06), pages 537-541, XP002924247	3,4
X	----- YEE W. ET AL.: "Glucocorticoid-induced tropoelastin expression is mediated via transforming growth factor-beta3" AMERICAN JOURNAL OF PHYSIOLOGY. LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, vol. 270, no. 14, 1996, pages L992-L1001, XP002961278 ISSN: 1040-0605 the whole document -----	1,2

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International application No.  
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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 8-11 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12, all partially

Oligonucleotides having a sequence at least 80% identical to a subsequence of SEQ ID NO:1 or SEQ ID NO:2 (TGF-RII), as claimed in claims 1-4. Pharmaceutical preparations, uses and methods related thereto.

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2. claims: 1-12, all partially

Oligonucleotides having a sequence at least 80% identical to a subsequence of SEQ ID NO:94, SEQ ID NO:95 or SEQ ID NO:96 (TGF-R), as claimed in claims 1-4. Pharmaceutical preparations, uses and methods related thereto.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2005/001298

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03000656	A	03-01-2003	EP 1406915 A2 JP 2005504522 T US 2004147472 A1 US 2003064944 A1	14-04-2004 17-02-2005 29-07-2004 03-04-2003
WO 9319783	A	14-10-1993	AU 3943793 A US 5958411 A	08-11-1993 28-09-1999
EP 1133988	A	19-09-2001	AU 6010901 A WO 0168146 A2 JP 2003526684 T US 2003186906 A1	24-09-2001 20-09-2001 09-09-2003 02-10-2003